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# POPULATION TRENDS IN CIGARETTE SMOKING AND BLADDER CANCER[1, 2]

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Hoover, R. and P. Cole (Harvard Univ. School of Public Health, Boston, Mass. 02115). Population trends in cigarette smoking and bladder cancer. *Amer J Epidem* 94: 409–418, 1971.—An association between cigarette smoking and bladder cancer has frequently been demonstrated. The causal nature of the association has, however, remained in doubt. Because of this, trends in smoking habits and bladder cancer experience were examined for successive birth cohorts of men and women in the United States, Denmark and England and Wales. Increasing rates of the disease were observed in populations characterized by an increase in smoking among successive birth cohorts. The association is consistent in both sexes, different nationalities and in urban and rural groups. This makes it unlikely that the findings result from an association both of smoking and bladder cancer with a third variable.

bladder cancer; cohort analysis; smoking, cigarette

Periods of rapid rise or fall in the incidence of a disease may be fruitful periods for investigations of that disease's etiology, since such changes must be preceded by striking changes in the character or quantity of at least one causal factor.

Clemmesen (1) and Lockwood (2) suggested that the rapidly increasing incidence rate of bladder cancer seen in Denmark may have been due to an increase in smoking habits. Case (3) has suggested that the increasing mortality rates from this disease in English men might be following a cohort pattern. Recently, Cole et al. (4) pointed out that increasing bladder cancer incidence rates among American women parallel an increase in cigarette smoking by successive cohorts.

Although the association of bladder cancer risk and cigarette smoking is well established, it remains uncertain whether the association is causal. If the association is causal, increasing rates of the disease should be observed in populations characterized by an increase in smoking among successive birth cohorts. The absence of such relationships would argue against the causal nature of the association between smoking and bladder cancer. We have therefore reviewed the trends of bladder cancer and of smoking in successive birth cohorts in several populations.

## Methods

To correlate exposure and outcome in successive cohorts, reliable information on both over an extended period of time is required. The paucity of information on exposure limits the populations available for this type of analysis in the present context. Three populations for which this information is adequate are those of the United

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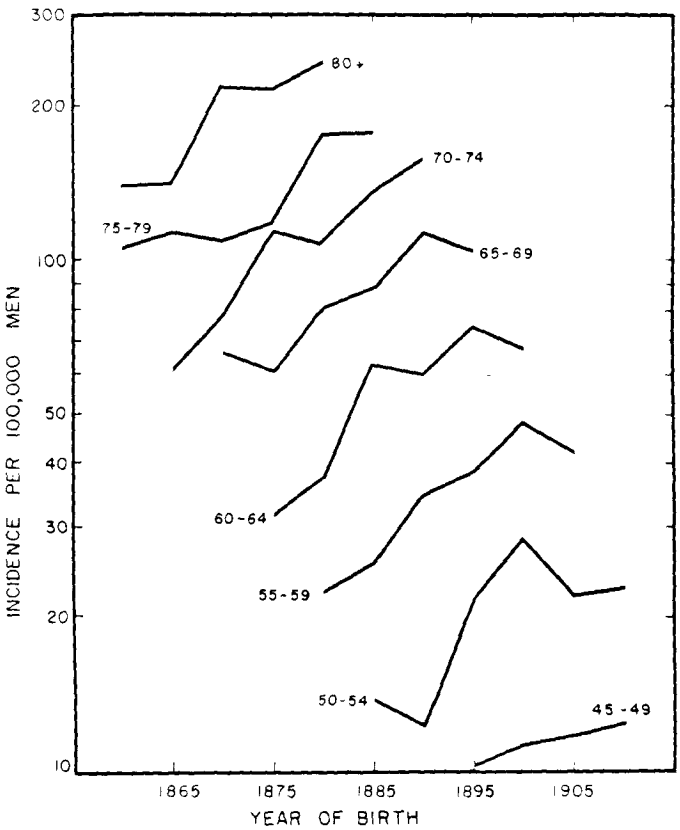


FIGURE 1. Annual incidence rates of bladder cancer by age for successive five-year birth cohorts of Connecticut men born between 1860 and 1910 (data from the Connecticut State Department of Health (7-9)).

States, Great Britain and Denmark. Data on smoking from all three countries have therefore been related to the most suitable measures of bladder cancer frequency available. These measures are incidence rates in the United States (Connecticut) and Denmark and mortality rates in England and Wales.

Estimates of the prevalence of smoking in successive cohorts are based on data from various national surveys. For the United States the proportions used for cohorts born after 1884 are estimates of the proportion of the cohort that will smoke in its lifetime. Such estimates were calculated from data collected during a national survey of smoking habits done in 1955 and are based on the proportion of people in each cohort who had ever smoked at the time of the survey (5). Estimates for cohorts born prior to 1885 are based on current smokers at the time of a survey done in 1947. For Denmark and Great Britain the proportions used are based on current smokers at the time of a national survey.

When estimates of a cohort's lifetime exposure rates were not available, it was assumed that the smoking pattern of a birth cohort, when surveyed, accurately reflected its relative lifetime cigarette smoking experience. Current smoking habits at the time of the survey will underestimate the exposure of older cohorts, since people in these cohorts will have had more time and more reasons for discontinuing the habit. However, available data (6) indicate that such underestimates are small enough not to affect any trends observed over successive cohorts. To avoid underestimating the exposure for younger cohorts, information is

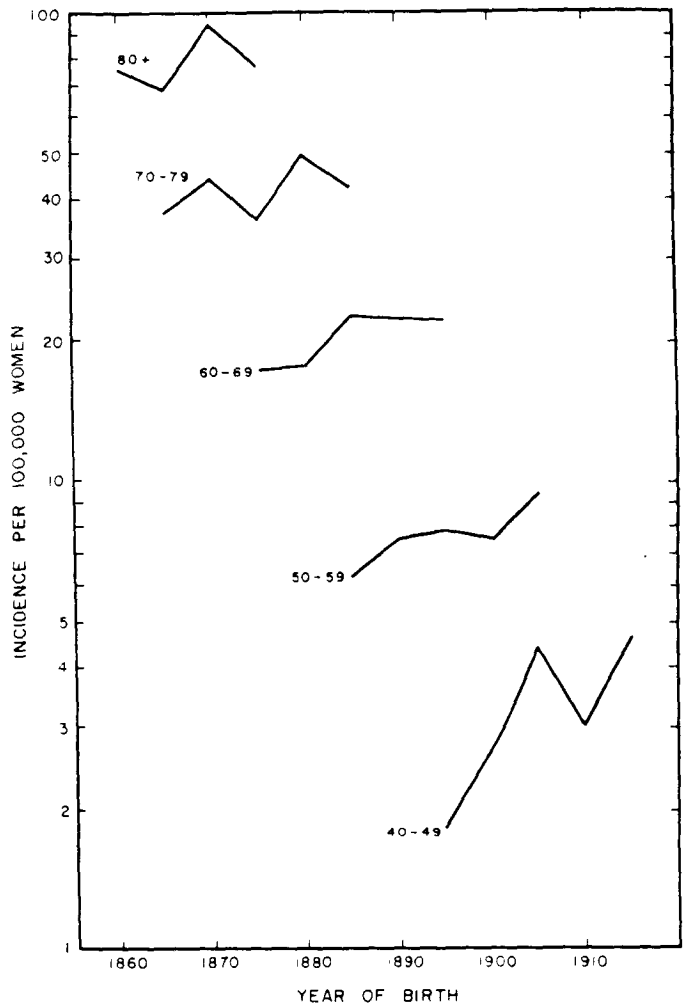


FIGURE 2. Annual incidence rates of bladder cancer by age for successive five-year birth cohorts of Connecticut women born between 1860 and 1915 (data from the Connecticut State Department of Health (7-9)).

used only from cohorts at least 30 years of age when surveyed, the age at which a cohort's smoking pattern becomes relatively fixed (5, 6).

## RESULTS

### *Bladder cancer trends*

United States: Age-specific trends in bladder cancer incidence rates by cohort for Connecticut men are presented in figure 1. The few data available for earlier cohorts suggest that the increase in incidence rates started with the cohorts of 1870 to 1880 (7–9). For men born subsequently, a cohort type of increase in rates (higher at every age for each successive cohort) is seen at least up until those born in 1905. Because bladder cancer is a disease of the elderly, relevant data for younger cohorts are not yet available. What is available for the 1905 and 1910 cohorts suggests a leveling off and possibly a decrease in age-specific incidences.

Figure 2 shows age-specific trends in incidence by birth cohort for Connecticut women. For stability, rates are presented in 10-year age groupings. There is a consistent

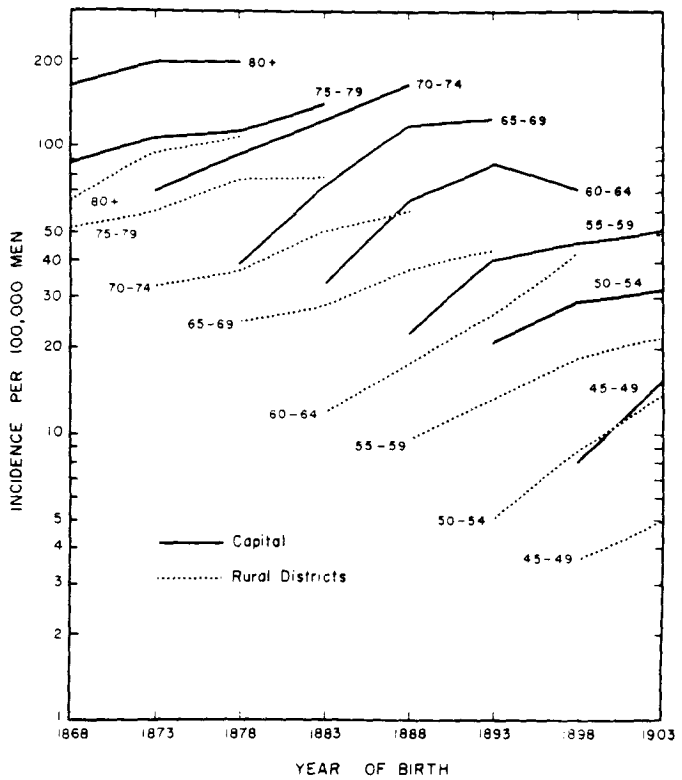


FIGURE 3. Annual incidence rates of bladder cancer by age for successive five-year birth cohorts of Danish men from the capital and from the rural districts born between 1868 and 1903 (data from Clemmesen (10, 11)).

upward trend in incidence rates beginning with the cohort of 1895.

Denmark: Perhaps the best illustration of increasing rates affecting successive cohorts occurs in the data for urban and rural Danish men (figure 3). The rates in the rural sections are uniformly lower than those in the Capital, but the same phenomenon of a cohort pattern of increasing rates after the cohort of 1868 is seen in both areas.

Age-specific incidence rates for women in the Capital of Denmark are presented in figure 4. Despite fluctuation there is a general upward trend in the rates—at least from the cohort of 1878 and onward. The data on rural Danish women, while also somewhat erratic, follow the same general trend as those of the urban women (10, 11).

England: Due to the lack of data on the incidence of bladder cancer over a long period of time in England, only mortality rates can be used. Data available for the period since 1955 extend Case's observations on mortality from bladder cancer among English men and reveal a pattern quite similar to that in the Connecticut incidence data (Figure 5).

Mortality data for English women have not shown any appreciable increase in bladder cancer death rates up to 1967 (12).

### *Smoking*

If the observed cohort patterns of rising incidence rates are to be consistent with patterns of cigarette smoking, then it would be expected that smoking started to become popular among Connecticut, British and urban Danish men with the cohort of about 1870. The percentage of cigarette smokers would also be expected to increase with

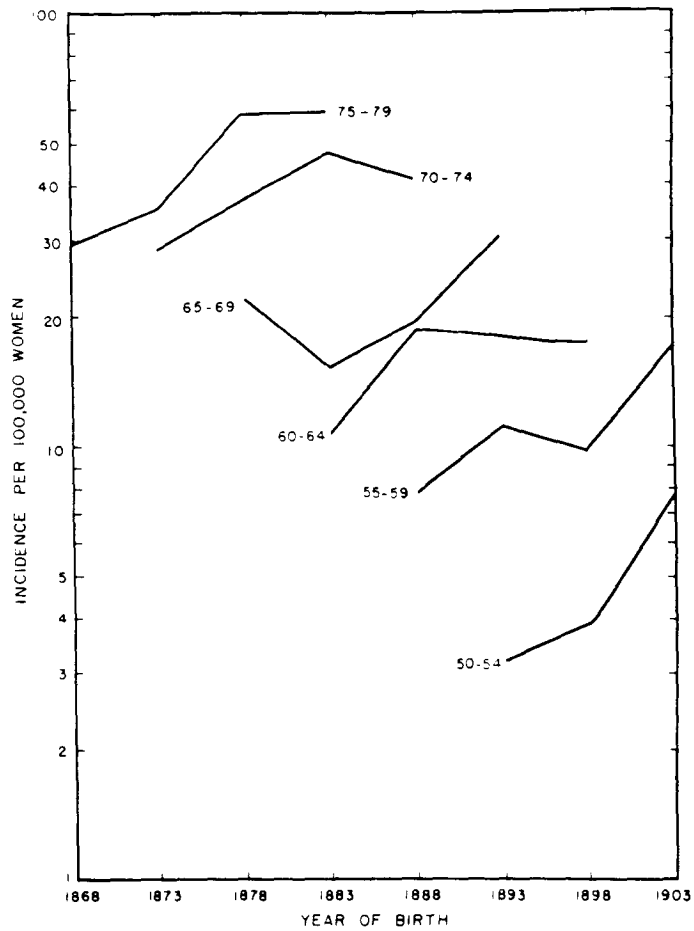


FIGURE 4. Annual incidence rates of bladder cancer by age for successive five-year birth cohorts of women from the capital of Denmark born between 1868 and 1903 (data from Clemmesen (10, 11)).

each successive cohort until that of about 1905 when it might level off in the United States and Great Britain. A similar pattern, beginning at a much lower baseline level and not leveling off with the more recent cohorts would be expected in the data on smoking for Danish women and rural Danish men. Cigarette smoking would be insignificant among United States women until the cohort of about 1895. Smoking would then be more popular in each successive cohort at least through the cohort of 1925. Finally, with no evident trend of bladder cancer mortality rates among British women, and in the absence of early incidence data, no prediction would be made about smoking habits other than a lack of trend prior to the cohort of 1880.

As is shown below, these trends in smoking habits are generally what is observed in published data.

United States: Data from Haenszel and Shimkin (5) provide exposure rates by cohort for the general population of the United States. Table 1 shows the per cent of women who have ever smoked by birth cohort. Among women born prior to about 1890 smoking was and is uncommon. However, a progressive rise in the per cent who ever smoked is noted from the 1886 cohort through the 1926 cohort. This corresponds with the general impression that cigarette

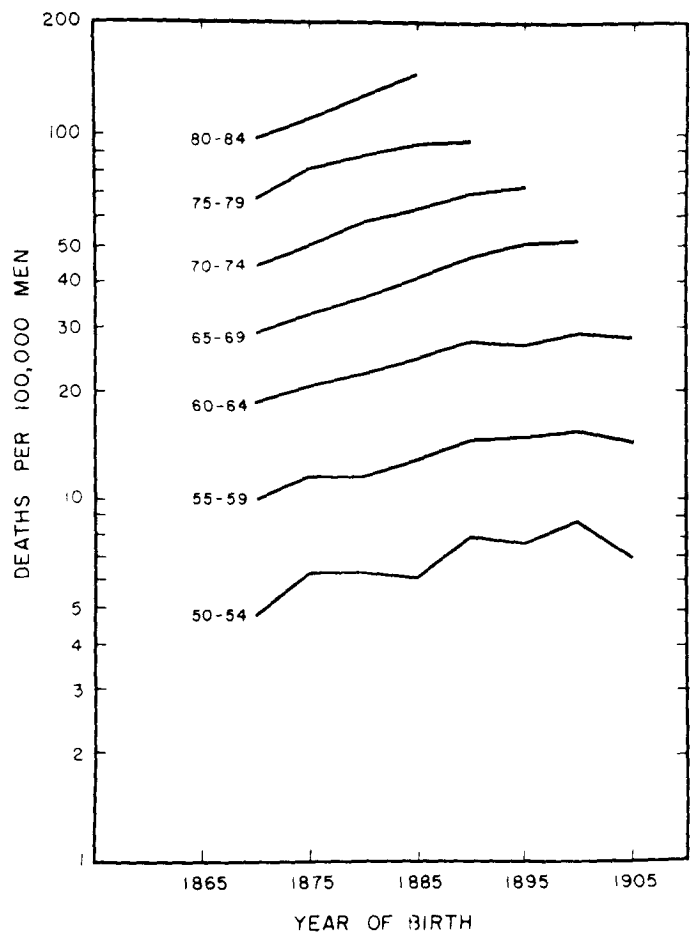


FIGURE 5. Annual mortality rate from bladder cancer by age for successive five-year birth cohorts of men from England and Wales born between 1865 and 1905 (data from Case (3) and the Registrar General (12)).

smoking became popular among women only after World War I (when the cohort of 1900 was in its 20's).

Relevant exposure data on men are more difficult to obtain. Due to the lack of population based surveys of smoking habits prior to 1955, data on smoking habits for cohorts born prior to 1890 are unreliable. Since the percentage of men having ever smoked cigarettes among the 1895 cohort is 56.6 per cent (5), it is apparent that the popularity of the practice began with an earlier cohort. Data collected in Columbus, Ohio in 1947 (13) and in Fortune magazine's national poll of 1935 (14) indicate that cigarette smoking began to gain popularity among men with the cohort of 1870. At the time of the surveys only 5 per cent of men born prior to 1865 smoked cigarettes regularly, while about 40 per cent of men born in 1880 and later were regular smokers. Figure 6 illustrates the percentage of men who were cigarette smokers by birth cohort. A progressive increase with each successive cohort is noted until a leveling off with the cohort of 1910.

Denmark: Data for Danish women are presented in table 2. The data are sufficient for indicating the trend in cigarette smoking. However, when comparing them with the percentages from the United States it should be noted that the Danish figures are

based on "present smokers" at the time of the survey while data from the United States are estimates of lifetime exposure. When this is taken into account the apparent earlier and heavier exposure of Danish women becomes even more striking. In fact, comparing the per cent of present smokers among United States women (5) with the Denmark data shows the percentages for Danish women to be one third higher for each cohort. Furthermore, the Danish figures for heavy smokers are consistently greater for each cohort than the comparable United States percentages (5, 15). A further observation is that cigarillo smoking (table 2) was popular in older Danish women but not present in England or the United States.

Figure 6 illustrates the smoking experience of Danish men. Again, the data are rates of current smokers at the time of the survey. This results in an underestimation of the absolute values of the proportions of persons who ever smoked, but has little effect on the trends of the rates. These are strikingly similar to those in the United States and England. The leveling off of per cent of smokers with the cohort of 1915, however, is not seen among rural men.

England: Trends in English women's smoking habits by cohort parallel those of women in the United States (table 1). Cigarette smoking by men is also similar to that in the United States and Denmark as is demonstrated in figure 6 for present smokers. In England, there is an actual decline in the per cent of smokers with the cohort of 1910.

Analyses were also done using the proportion of heavy smokers as the index of exposure wherever the values were available. The results obtained were entirely compatible with those presented above.

### *Analytic considerations*

Although the quality and representativeness of the data on exposure are probably adequate for descriptive purposes, they are not adequate for extensive quantitative analyses. However, the regression of bladder cancer incidence on proportion of smokers by cohort, controlling for age, was computed, using the data on Connecticut men. Connecticut men were chosen for this analysis because they comprise the group on whom data are most complete. The slope of the regression line was 1.87 with a standard error of 0.29 ($p < 0.001$).

TABLE 1

*Percentage of women cigarette smokers in successive 10-year birth cohorts in the United States and Great Britain*

| Birth cohort* | United States† | Great Britain‡ |
|---|---|---|
| 1881–1890 | 4.6 | 18.2 |
| 1891–1900 | 12.6 | 32.8 |
| 1901–1910 | 26.7 | |
| 1911–1920 | 40.5 | 45.9 |
| 1921–1930 | 47.8 | 51.0 |

* The surveys used similar age classifications but were done six years apart so the British data have been approximated to the United States cohort classification (e.g. the percentage listed for the 1911–1920 cohort in Great Britain actually refers to the cohort of 1905–1914).

† Estimates of the maximum percentage of the population in a cohort who would smoke cigarettes at some time in their lives (data from Haenszel and Shimkin (5)).

‡ Percentage of the population in a cohort who were cigarette smokers during the first quarter of 1949 (data from Hulton Research (16)).

## Discussion

Case pointed out in 1956 that increasing bladder cancer mortality rates among English men resulted from higher mortality rates at every age for each successive birth cohort (3). The only two exposures known to be associated with bladder cancer are smoking and certain occupations. The increase in rates could not be attributed to a specific changing exposure because it was not known how much of the disease in any one population might be attributable to either of the suspected causes.

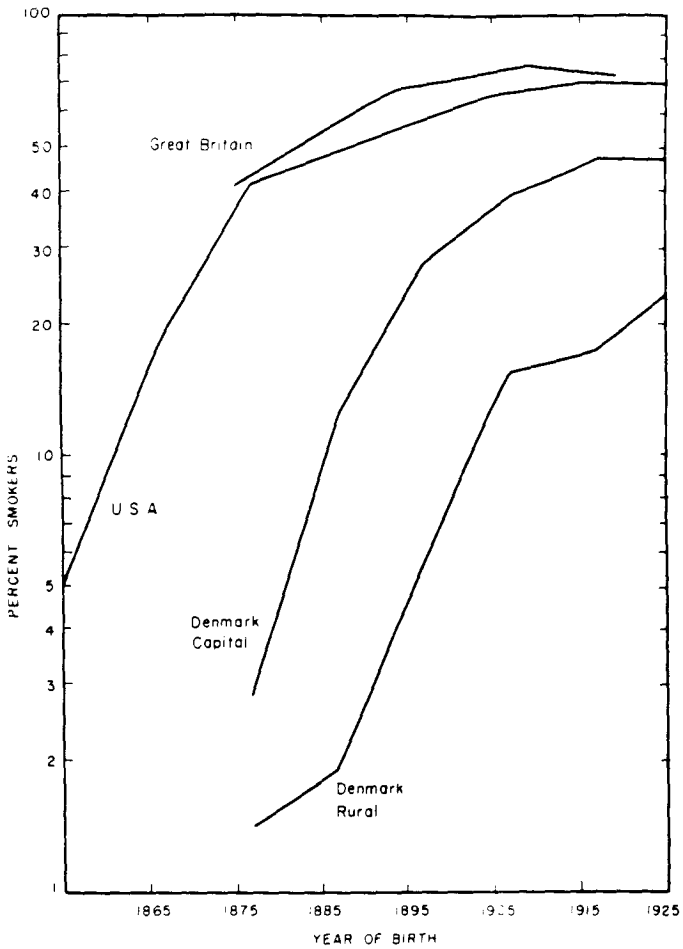


FIGURE 6. Percentage of cigarette smokers by cohort for men in Great Britain*, the United States† and the capital and rural areas of Denmark‡.

* Percentage of the population in a cohort who were cigarette smokers during the first quarter of 1949 (data from Hulton Research (16)).

† Values prior to 1885 are the percentages of current smokers in a cohort at the time of a survey done in 1947 (data from Mills and Porter (13)). Values from 1885 onward are estimates of the lifetime maximum percentage of the population in a cohort who smoked cigarettes at some time in their lives (data from Haenszel and Shimkin (5)).

‡ Percentage of current smokers at the time of the Danish National Morbidity Survey, 1952–53 (data from Hamtoft and Lindhardt (15)).

However, even without knowledge of these attributable risks there was evidence that might have allowed implication of smoking as the exposure responsible for these cohort increases in rates. It could be presumed that any increase in the use of carcinogenic substances by industry would affect all ages in the work force (18 to 65) equally. This would produce more a cross-sectional type of increase than a cohort pattern. For a cohort type of increase to result from occupational exposures it would be necessary that the exposure acted differently at different ages, i.e., more carcinogenic for younger persons. While this is possible, it seems unlikely to have occurred to the extent required to produce the observed effect. Since occupation is unlikely, only smoking and other as yet unknown exposures remain to account for the cohort type

of increase in bladder cancer rates. From various studies of smoking it appears both that amounts and types of smoking are themselves cohort phenomena with a particular cohort's habits well established by about age 30. In the absence of knowledge of other causal exposures it would seem reasonable to attribute the increase in bladder cancer rates to smoking since trends in the exposure and disease rates of a cohort have been shown to be parallel.

This position was supported by the Massachusetts study (4, 17). This study provided estimates of attributable risks per cent for smoking, occupation and as yet unknown exposures for bladder cancer in an industrialized United States population. These percentages were, respectively, 39, 18 and 43 for men and 29, 6 and 65 for women. Smoking therefore appears to be the major recognized factor associated with bladder cancer in this population, considerably overshadowing the influence of occupation.

Of course, the usual precautions when considering the causal nature of an association must be kept in mind. It may be that the increase in bladder cancer rates reflects increased ascertainment of the disease in this not easily accessible organ. For this to produce the observed cohort type of increase, it would be necessary that the improvement in ascertainment acted differentially on different cohorts. Furthermore it must have gone on simultaneously in rural and urban Denmark and must have begun to occur in relation to USA women some 30 years after it began in USA men. While each of these conditions is plausible, taken together they would seem quite unlikely. There is also the matter of 40–65 per cent of the disease remaining unaccounted for by known exposures (4, 17). However, to cause the observed pattern of increasing rates, an unknown exposure would also have to parallel the patterns of disease frequency demonstrated here. While possible, until such a factor is identified and shown to fulfill this requirement it would seem wise to consider smoking as the exposure responsible.

TABLE 2

*Percentage of women smokers in successive birth cohorts in urban and rural Denmark**

| Birth cohort | Capital | | Rural districts | |
|---|---|---|---|---|
| | Cigarettes | Other† tobacco | Cigarettes | Other† tobacco |
| Before 1883 | 6.4 | 20.3 | 0.3 | 1.7 |
| 1883–1892 | 12.2 | 19.8 | 2.9 | 5.3 |
| 1893–1902 | 22.8 | 22.8 | 10.8 | 6.3 |
| 1903–1912 | 37.2 | 11.8 | 18.3 | 3.9 |
| 1913–1922 | 55.3 | 3.5 | 35.7 | 2.9 |
| 1923–1932 | 62.7 | 0.6 | 48.4 | 2.3 |

* Percentages refer to current smokers at the time of the Danish National Morbidity Survey, 1952-53 (data from Hamtoft and Lindhardt (15)).

† Almost exclusively cigarillos.

Cohort-specific bladder cancer rates may have leveled off or actually begun to decline in the most recent cohorts of men. It is tempting to relate this to the leveling off of per cent of cigarette smokers and to the decline of the per cent of heavy smokers in the most recent cohorts (5, 15, 16). However, it is too early for this to be determined. The decline in percentage of heavy smokers is small and the decline in bladder cancer rates appears in slightly earlier cohorts than does the leveling off of per cent smokers.

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